The Stereochemistry of Sesamolin

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Spectroscopic evidence is presented to confirm the structure (1) of the lignan sesamolin. The results, in conjunction with earlier chemical evidence, define its absolute stereochemistry. An alternative mode of biosynthesis is proposed.

SESAMOLIN is a unique lignan of the 'furanofuran' type;[1] chemical support for the acetal structure (I), first suggested[2] in 1936, has been obtained by several groups of workers.[3-6] Degradation to the nitro-lactone (V)[5,6] provided evidence not only of the close structural relationship with the co-occurring lignan sesamin (11a) but also gave proof of an identical stereochemistry at C-1, C-5, and C-6 in the 3,7-dioxabicyclo[3,3,0]octane skeleton. Spectroscopic measurements now provide additional support for the structure (I) and permit the final definition of the stereochemistry at C-2.

The mass spectrum of sesamolin is remarkably simple and shows a molecular ion (*m/e* 370) accompanied by three major fragment ions (*m/e* 233, 203, and 138). Two of the latter result presumably from fission in the expected fashion at the acetal linkage of (I) to give ion (III), *m/e* 233, and, after proton capture, the sesamol ion (IV), *m/e* 138. The 100 MHz ^{1}H n.m.r. spectrum shows signals for the three aromatic protons of the 4-hydroxycatechol methylene ether (sesamol) ring distinct from those of the dioxole ring (τ 3·15—3·25): τ 3·35 (d, J 8·8 Hz, H_A), 3·56 (dd, J 3·8 and 8·8 Hz, H_B), and 3·44 (d, J 3·8 Hz, H_C). The spectrum of the 3,7-dioxabicyclo[3,3,0]octane system is capable of a first-order analysis (see Table) and is in accord with the

[1] R. D. Haworth, *J. Chem. Soc.*, 1942, 448.
[2] J. Boesken, W. D. Cohen, and C. J. Kip, *Rec. Trav. chim.*, 1936, **55**, 815.
[3] M. Beroza, *J. Amer. Oil Chemists Soc.*, 1950, **27**, 164.
[4] M. Beroza, *J. Amer. Chem. Soc.*, 1955, **77**, 3332.
[5] H. Erdtman and Z. Pelchowicz, *Chem. and Ind.*, 1955, 567.
[6] E. Haslam and R. D. Haworth, *J. Chem. Soc.*, 1955, 827.

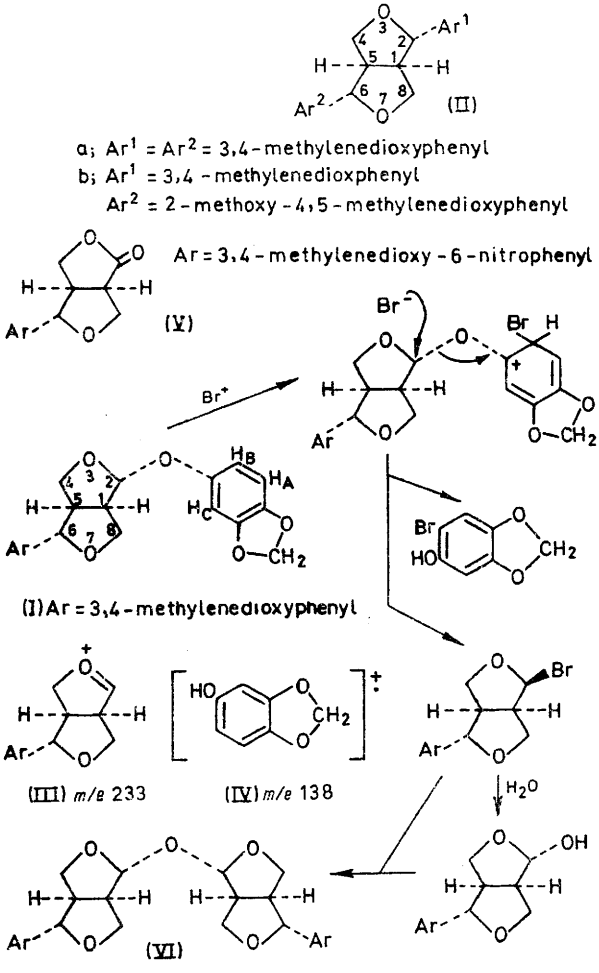
previously designated structure and stereochemistry. Despite the fact that in related work [7,8] it has not been possible to use the Karplus equation directly with this system to make stereochemical assignments, the slightly broadened singlet at τ 4·57 for H-2 in the spectrum of (I) can only indicate that this proton occupies an ' axial ' position and is *trans* to H-1. The acetal linkage at C-2 probably produces local shielding effects and possibly some distortion of the normal geometry of the skeleton particularly at C-2 and C-1. Thus in the spectrum of (I) the signals due to the 4-, 5-, and 6-protons are very similar to those of sesamin but those from the 1- and 8-protons are different (see Table).

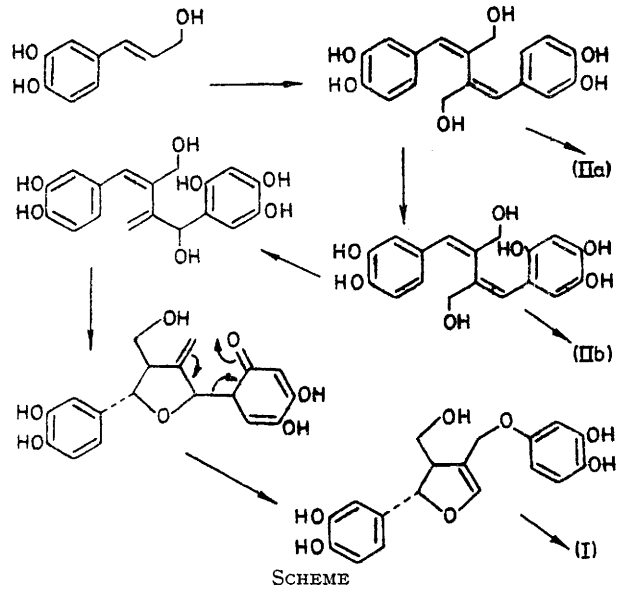
Disaminyl ether (VI) was obtained [6] by bromination of sesamolin in acetic acid. Both ^{1}H n.m.r. and mass spectral data confirm the suggested structure and permit a logical mechanism for its formation to be proposed. The mass spectrum of (VI) shows a molecular ion (*m/e* 482) and again a simple fragmentation pattern, with principal fragments at *m/e* 249, 233, and 203. The ion (III), *m/e* 233, and that at *m/e* 249 result from fragmentation at the bond adjacent to the central oxygen atom in the symmetrical structure. This symmetrical feature of the structure (VI) is also borne out by the ^{1}H n.m.r. data: the spectrum closely resembles that of sesamolin (I). The stereochemistry at C-2 of (VI) must be identical with that in sesamolin (see Table) and hence the formation of disaminyl ether in the bromination probably involves a double inversion at C-2 along with the introduction of adventitious water.

N.m.r. data *

	Sesamin (IIa) †	Sesamolin (I)	Disaminyl ether (VI)	Nitro-lactone (V)
H-1	7·12 (m)	6·80 (q, *J* 8·5)	7·05 (q, *J* 8·5)	6·90 (m)
H-5		7·15 (m)	7·21 (m)	
H-2	5·25 (d, *J* 4·0)	4·57 (s)	4·75 (s)	
H-6		5·72 (d, *J* 5·5)	5·68 (d, *J* 5·5)	4·4 (d, *J* 2·0)
H-4*a*	6·26 (dd, *J* 4·0 and 8·5)	6·12 (dd, *J* 2·0 and 8·5)	6·15 (m)	5·35 (d, *J* 6·0)
H-4*e*	5·90 (dd, *J* 6·0 and 8·5)	5·93 (dd, *J* 6·0 and 8·5)		5·35 (d, *J* 6·0)
H-8*a*		6·45 (dd, *J* 8·0 and 8·5)	6·48 (dd, *J* 7·5 and 8·5)	5·60 (dd, *J* 3·0 and 8·5)
H-8*e*		5·63 (t, *J* 8·5)	5·68 (t, *J* 8·5)	5·80 (dd, *J* 6·0 and 8·5)

* τ values; internal standard tetramethylsilane; solutions in deuteriochloroform; 100 MH_3 spectra; *J* in Hz. † Coupling constants obtained by spin decoupling; H-1 ≡ H-5, H-2 ≡ H-6, H-4 ≡ H-8.





SCHEME

[7] E. D. Becker and M. Beroza, *Tetrahedron Letters*, 1962, 157.
[8] A. J. Birch, P. L. Macdonald, and A. Pelter, *J. Chem. Soc.* (*C*), 1967, 1968.

The structure of sesamolin remains unique amongst lignans. Erdtman and Pelchowicz [5] in 1955 put forward a biosynthetic route for its formation. An alternative oxidative sequence, which has interesting biosynthetic implications, takes note of the occurrence of sesangolin (IIb) [9] with sesamin (IIa) and sesamolin (I) in the oil expressed from the seed of *Sesamum angolense* and is shown in the Scheme.

[9] W. A. Jones, M. Beroza, and E. D. Becker, *J. Org. Chem.*, 1962, **27**, 3232.

EXPERIMENTAL

Samples were isolated as described previously.[6] Mass spectra were obtained at 70 ev with an A.E.I. MS12 spectrometer. ^{1}H N.m.r. spectra were determined with a Varian 100 MHz spectrometer.

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